4070-Pos Board B798
Computational Studies of the Catalytic Mechanism of the Staphylococcus Aureus Sortase a Enzyme
Pooja Shrestha, Jeff Wereszczynski.
Physics, Illinois Institute of Technology, Chicago, IL, USA.
When surface proteins are attached to the cell wall of Gram-positive bacteria, they play important roles in multiple pathogens such as pneumonia, meningitis, osteomyelitis, and so on. Class A sortase (SrtA) enzymes play a key role in the insertion of surface proteins into the cell wall. StrA recognizes an LPXTG sorting signal motif in a target protein and catalyzes a transpeptidation reaction that joins it to a Lipid II molecules that will be embedded into the cell wall. Bacteria strains that lack SrtA are incapable of placing surface proteins, suggesting that SrtA may be a novel drug target for therapeutics against Gram-positive bacteria. However, the precise mechanism of transpeptidation is not well understood because of the unstable catalytic intermediates. Here we report on a series of molecular dynamics simulations using a hybrid quantum mechanical/molecular mechanics (QM/MM) approach to investigate the catalytic mechanism of SrtA.

4071-Pos Board B799
Investigations of Model Proton-Coupled Electron Transfer Reactions from a Mixed Quantum-Classical Liouville Perspective
Farnaz Shakib, **Gabriel Hanna**.
Department of Chemistry, University of Alberta, Edmonton, AB, Canada.
Many biological processes involve the transfer of electrons from a donor to an acceptor accompanied by the transfer of protons. This phenomenon, known as proton-coupled electron transfer (PCET), is at the heart of energy conversion reactions in photosynthesis and respiration. Theoretical methods, which treat the coupled dynamics of the transferring protons, electrons, and their environment in a quantum mechanical fashion, are required for accurately describing PCET reactions. However, the size and complexity of real systems render the application of a full quantum treatment computationally impossible. Hybrid methods which treat the transferring protons and electrons quantum mechanically, but treat the donor, acceptor, and solvent molecules classically, offer feasible yet accurate alternatives to full quantum treatments. In this study, for the first time, we adopt a surface-hopping approach based on the solution of the quantum-classical Liouville equation (QCLE) for the study of PCET reactions. The advantage of this approach over other nonadiabatic dynamics methods is that it inherently accounts for quantum coherence effects in the dynamics through phases accumulated during trajectory segments on the means of two adiabatic surfaces. As a starting point, we consider a simple model, which is comprised of three coupled degrees of freedom: an electronic coordinate, a protonic coordinate, and a solvent coordinate. Varying the parameters in the model allows us to study both concerted and sequential PCET mechanisms. For each mechanism considered, we investigate the role played by mean surface evolution in an ensemble of surface-hopping trajectories and discuss the implications of decoherence of the proton-electron subsystem on the rates of these reactions.

4072-Pos Board B800
New Insights on Interactions of a Quantum Vibration with an Environment of Hydrogen-Bonded Groups from the Mixed Quantum-Classical Liouville Approach
Holly Freedman, Gabriel Hanna.
Chemistry, University of Alberta, Edmonton, AB, Canada.
How the energy released during ATP hydrolysis can perform work in proteins despite being weak and short-lived has been a long-standing open question in biology. To address this "crisis in bioenergetics", A.S. Davydov proposed a quantum mechanical model by which amide I vibrational excitations couple to alpha-helical phonon modes in such a way as to facilitate energy storage and propagation. Because of the computational expense associated with fully quantum mechanical treatments of systems with many degrees of freedom, practical simulations of the Davydov-Scott model may be realized via a mixed quantum-classical approach. We take a novel mixed quantum-classical approach to this problem by implementing two methods for solving the mixed quantum-classical Liouville equation, a surface-hopping solution and an approximate, mean-field-like solution in which the quantum subsystem is described in terms of continuous variables. The time-scale of vibrational delocalization is investigated for a one-dimensional model of a protein alpha helix. Results from the surface-hopping model suggest that population transfer between distal sites may occur in the case of an asymmetric potential, although no transfer occurs if the vibrational excitation is treated by a mean-field description.

4073-Pos Board B801
Phosphoryl Transfer Transition State Computationally Modeled by Mgf3(-) in the Oncogenetically Indicated Gtpase Protein Rhoa and it's Activating Protein Rhoa.Gap
Whitney F. Kellett, Nigel G.J. Richards.
Chemistry and Chemical Biology, Indiana University Purdue University Indianapolis, Indianapolis, IN, USA.
GTPase enzymes, which hydrolyze guanosine triphosphate (GTP) to guanosine diphosphate (GDP) and inorganic phosphate (P_i), are involved in a large number of critical cellular processes including proliferation. GTPase Activating Protein (GAP) is responsible for the regulation of GTPase. GTPase proteins, when poorly regulated, can signal for uncontrolled cellular growth and are indicated in oncogenesis [1].
I present a computational model of the GTPase protein RhoA in solution and bound to the regulating protein RhoA.GAP. I have modeled a transition state analog of the GTP to GDP phosphoryl transfer reaction based on the crystal structure of the RhoA:RhoGAP protein complex with GDP and MgF_3^- [2]. Hybrid QM/MM Car-Parrinello MD simulations were performed on the protein complex with the transition state analog, all in explicit water. The reaction was modeled using thermodynamic integration by increasing the terminal phosphate-oxygen bond.
These simulations provide evidence for a dissociative transition state and suggest that MgF_3^- is the best adduct to date to model the transition states of these types of enzymatic phosphoryl transfer reactions. This model could be further exploited to design transition state mimics for many families of GTPase proteins. Finally, this model has shown some structural effects of binding the RhoA.GAP protein to RhoA. These preliminary results indicate that we can understand better the RhoGAP:RhoA protein interface using computational methods. This model could be further exploited to identify ways to dissociate the errant GTPase:GAP complex by targeting the GTP binding site or even the protein-protein interface itself.

4074-Pos Board B802
Quantitative Interpretation of Chemical Shifts Enables Mapping Proteins Conformational Landscape
Alessandro Cembran, Gianluigi Veglia.
Chemistry, University of Minnesota, Minneapolis, MN, USA.
To carry out their function, most proteins need to undergo transitions among different states. Understanding how the equilibrium between different states is altered upon ligand binding or interaction with other biological partners is of critical importance to explain protein function.
Nuclear Magnetic Resonance isotropic ^1H and ^{15}N chemical shifts are a sensitive probe for both protein structure and conformational dynamics, and thus are an ideal observable to monitor equilibrium shifts. Yet, noise in the peak positions complicates the quantitative correlation of chemical shifts to the equilibrium position. Here we propose a robust methodology that relies on statistical analysis of NMR $^1H/^{15}N$ HSQC data and provides a quantitative measure of the equilibrium shift associated to ligand or substrate binding. In short, linearity in the $^1H/^{15}N$ chemical shifts position across different protein constructs is first identified by principal component analysis. Then, the scores of all residues on their principal components are filtered and combined together, and the shift in equilibrium position for each state is given in terms of confidence intervals. Finally, the degree of collectiveness of the protein response to ligand binding is mapped onto the protein structure by applying an adapted version of the chemical shifts covariance analysis (CHESCA). We illustrate the method in its applications to ligand binding to protein kinase A (PKA) and to a series of mutants of phospholamban. The results show that the method is capable of discerning the multiple states populated upon binding of different ligands to PKA as well as the shift in equilibrium position induced by mutations of phospholamban serine 16. Noticeably, the CHESCA analysis shows that while PKA response is highly collective throughout the whole protein, the PLN response is collective only in the surroundings of the perturbed region (domain 1A).

4075-Pos Board B803
Electronic Structure Study of Certain Rhizoferrin Analogs and Its Ferric-Ion Complexes
Archana Dubey[1], Olle Heinonen[2].
[1]Physics, UCF, Orlando, FL, USA, [2]Materials Science Division, Argonne National Laboratory, Lemont, IL, USA.
We have used first-principles electronic structure methods to examine the ferric-ion binding specificity of rhizoferrin analogs: (a) the *homo-rhizoferrin and nor-rhizoferrin* that fall in the category of variable length diamine bridge; (b) *monodesoxy-rhizoferrin* and *didesoxy-rhizoferrin* having different functional groups in the citric-acid moieties of rhizoferrin, and (c) *cyclized*